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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,215	04/07/2004	Eric J. Benjamin	AM101252	7245

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EXAMINER	
COLEMAN, BRENDA LIBBY	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 11/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/820,215	BENJAMIN ET AL.	
	Examiner	Art Unit	
	Brenda L. Coleman	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-56 are pending in the application.

This action is in response to applicants' amendment filed September 6, 2006. Claims 33 and 56 have been amended.

Response to Amendment

Applicant's amendments filed September 6, 2006 have been fully considered with the following effect:

1. With regards to the 35 U.S.C. § 112, first paragraph rejection of claims 1-56 labeled paragraph 1 of the last office action, the applicants' arguments have been fully considered, however they were not found persuasive. Applicants' state that no evidence has been presented that there is any reason to doubt that a skilled artisan would doubt that the intranasal compositions of the invention would not be useful in preventing such tolerance, especially in light of the fact that NMDA receptor antagonists are known to prevent the opiate analgesia tolerance. See, for example, the Trujillo abstract (enclosed). However, Trujillo does not state that NMDA receptor antagonists prevent the tolerance to opiate analgesia. Additionally, Brown et al., Current Topics in Medicinal Chemistry states that the study of NMDA antagonists in a variety of neuropathic pain models only suggests that they **may be** useful for **treating** the pathological conditions underlying neuropathic pain. While the specific diseases listed in claims 10, 13, 14, 16, 18, 20, 22, 24, 42, 44, 45, 47, 49, 51 and 53 have been indicated by the applicants to have a nexus with NMDA, this does not provide enablement for those diseases and/or disorders listed. Not all diseases and/or

disorders are treatable, let alone preventable. Where structure sensitivity exists (in the pharmaceutical art) degree of testing must be representative of claims' scope. Note In re Fisher 166 USPQ 18; In re Surrey 151 USPQ 724. The recent journal article, i.e. Brown et al. (2006), provided by the applicant in their response filed September 6, 2006 indicates that deleterious side-effects observed with many of the compounds in clinical trials have raised the question if this is a mechanism-based effect which cannot be overcome. Furthermore, Brown states that it appears that within the non-competitive class of NMDA receptor antagonists, the most potent compound (e.g. MK-801) are unsuitable for clinical use due to the side effect profile.

While Brown et al., indicates that the use of memantine a clinically available (Parkinson's disease and more recently Alzheimer's disease) NMDA antagonist hs demonstrated a superior side-effect profile, but did not show efficacy in several modesl of clinical pain. Thus the uses being urged are not in currently available form based on the activity relied on and the specification provides only a starting point for further research. Note Genentech vs. Novo Nordisk 42 USPQ 2d 1001.

Claims 1-56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and stated above.

2. The applicants' amendments and arguments are sufficient to overcome the 35 USC § 112, second paragraph rejections labeled paragraph 2b), c) and d) of the last

office action, which are hereby **withdrawn**. However, with regards to the 35 U.S.C. § 112, second paragraph rejection labeled 2a) of the last office action, the applicant's amendments and remarks have been fully considered but they are not persuasive.

a) The applicant's stated that with respect to the phrase "pain relieving agent" a skilled artisan would have no difficulty understanding the meaning of the phrase. The phrase "pain relieving agent" is unduly functional. Names, structures, and chemical Formulae precisely define organic molecules. Attempting to define structure by function is not proper when the structures can be clearly expressed in terms that are more precise. Additionally, it is not sufficient to define a chemical structure solely by its principal biological property.

Claims 25 and 54 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record and stated above.

3. The applicants' amendments and arguments are sufficient to overcome the 35 U.S.C. § 102, anticipation rejections labeled paragraph 3), 4), 6) and 7) of the last office action, which are hereby **withdrawn**.

4. With regards to the 35 U.S.C. § 102(b) anticipation rejection of claims 1-26 by LIN, labeled paragraph 5) in the last office action, the applicant's amendments and remarks have been fully considered but they are not persuasive. The applicants' stated that EP-B1-0,778,023 only discloses [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-l(7)-en-2-yl)ethyl] phosphonic acid (EAA-090) and other NMDA antagonists. It is disclosed that

the compounds of the invention (rapamycin and NMDA or AMPA antagonist) may be administered orally or rectally. It is further disclosed that can be administered via "intramuscular, intraperitoneal, or subcutaneous injection" or intravenously. Finally, it is disclosed that rapamycin may be administered via intranasal or intrabronchial inhalation or insufflation. EP-B1-0,778,023 is silent with respect to intranasal administration or compositions of the NMDA antagonists. However, this is not so, EP-B1-0,778,023 includes within the scope of the invention the combination of rapamycin with NMDA and/or AMPA antagonists of which [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-l(7)-en-2-yl)ethyl] phosphonic acid (EAA-090) is specifically mentioned. EP-B1-0,778,023 teaches the administration by intranasal or intrabronchial inhalation or insufflation. The compositions and method of use of the compounds of the instant invention which **comprises** [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-l(7)-en-2-yl)ethyl] phosphonic acid (EAA-090) of which is open ended and may be anticipated by compositions which contains other components such as rapamycin.

Claims 1-26 are rejected under 35 U.S.C. 102(b) as being anticipated by LIN et al., EP 0 778 023, for reasons of record and stated above.

5. With regards to the provisional obviousness-type double patenting rejection as being unpatentable over copending Application No. 10/969,715 of the last office action, the applicants requested that this rejection be held in abeyance at this time.

Claims 1-9 and 26 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 26-29 of copending Application No. 10/969,715, for reasons of record.

6. With regards to the provisional obviousness-type double patenting rejection as being unpatentable over copending Application No. 10/820,216 of the last office action, the applicants requested that this rejection be held in abeyance at this time.

Claims 27-55 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11-28 of copending Application No. 10/820,216, for reasons of record.

7. With regards to the provisional obviousness-type double patenting rejection as being unpatentable over copending Application No. 10/961,871 of the last office action, the applicants requested that this rejection be held in abeyance at this time.

Claims 27-56 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-95 and 104-108 of copending Application No. 10/961,871, for reasons of record.

8. With regards to the provisional obviousness-type double patenting rejection as being unpatentable over copending Application No. 10/267,159 of the last office action, the applicants requested that this rejection be held in abeyance at this time.

Claims 21-24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 37-53 and 57-73 of copending Application No. 10/267,159, for reasons of record.

In view of the amendment dated September 6, 2006, the following new grounds of rejection apply:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claims 27-30, 33 and 34-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a) Claims 27-30 and 34-55 are vague and indefinite in that it is not known what is meant by a C_6 to C_2 alkylaryl in the definition or R_6.

b) Claims 27 and 55 recite the limitation "5 to 13 carbon atoms in the aryl moiety" in the definition of R_6. There is insufficient antecedent basis for this limitation in the claim.

c) Claim 33 is vague and indefinite in that it is not known what is meant by phosphahep-t-1-yl in the species labeled e).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda L. Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brenda Coleman

Brenda L. Coleman
Primary Examiner Art Unit 1624
November 17, 2006